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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,844	05/14/2001	Yi Hu	LEX-0176-USA	8344

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EXAMINER
RAMIREZ, DELIA M

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 12/02/2002 13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/854,844	HU ET AL.	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-8 are pending.

Applicant's addition of claims 5-8 in Paper No. 12, filed on 9/10/2002 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Priority

1. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/205275 filed on 5/18/2000.

Oath/Declaration

2. The oath or declaration was objected to in Paper No. 7, mailed on 12/3/2001 since it is defective. The citizenship of Inventor Olson is missing. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

Claim Rejections - 35 USC § 101

3. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-8 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

5. Claims 1-8 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

6. These rejections, which were discussed in previous Office Actions Paper No. 7, mailed on 12/3/2001 and Paper No. 10, mailed on 5/7/2002, were applied to claims 1-4 and are now applied to new claims 5-8 for the reasons of record.

7. Applicants have extensively argue that the polynucleotides of the instant invention have substantial, credible, specific and well-established utility. Applicants have submitted an alignment of the amino acid sequence of SEQ ID NO: 2 against the polypeptide encoded by the polynucleotide disclosed in GenBank's accession number XM_093852, which according to Applicant's opinion should be sufficient to show that Applicant's invention encodes a serine protease. Furthermore, Applicants argue that the present invention can be used in DNA chips as evidenced by hundreds of issued patents and that one of skill in the art does not need to know the substrate or specificity of the claimed polypeptide. Applicants assert that since proteases are known to be associated with many cellular functions, the polynucleotides of the present invention can be used as specific markers of the human genome and that such markers are targets for the discovery of drugs. Furthermore, Applicants argue that the present nucleotides have a specific utility in mapping the protein encoding regions of the corresponding human chromosome. It is Applicant's opinion that the PTO has issued several patents on

polynucleotides that have not been directly associated with the function of the polypeptide they encode. Finally, Applicants direct the Examiner's attention to several patents where there are no working examples or examples of real-world utilities.

8. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. While it is agreed that the GenBank entry submitted by Applicants is highly homologous to the claimed polynucleotide, there is no evidence of its function other than being annotated as similar to a epidermis specific serine protease. There is no evidence that in fact the GenBank's entry is indeed a serine protease. As indicated in previous office Action Paper No. 7, the state of the art is unpredictable in regard to assigning function based on sequence homology. See the teachings of Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) and Broun et al. (Science 282:1315-1317, 1998) already discussed. In the absence of information such as the specificity or substrate of the serine protease encoded by the polynucleotide of SEQ ID NO: 1 or whether the polynucleotide of SEQ ID NO: 1 comprises the critical structural element which are required to display serine protease activity, one of skill in the art cannot reasonably conclude that the claimed polynucleotide encodes a serine protease. At best, one of skill in the art can only conclude that the polynucleotides of SEQ ID NO: 1 and GenBank's entry XM_093852 (locus LOC166414) are highly homologous.

In regard to arguments that one does not need to know the function of the polypeptide encoded by the claimed polynucleotides since the polynucleotide can be used in DNA chips for gene expression detection and drug discovery, such use does not constitute a substantial utility in view of the need of further research to identify or reasonably confirm a "real world" context of use. Even if Applicant's assertion of function is correct and the polynucleotide of the instant

invention is indeed a serine protease, there is no disclosure of its role in humans or how its expression or lack thereof correlates with any disease or abnormality. Without this information, it is unclear how one of skill in the art can reasonably use this polynucleotide in drug discovery.

In regard to specific utility in mapping the protein encoding regions of the corresponding human chromosome, it is noted that if the function of the target polynucleotide is unknown, there is no specific utility for the polynucleotide of the instant invention as a probe. In response to arguments that the PTO has issued several patents on polynucleotides which do not have a specific function associated with them or patents which lack real-world utility or working examples, Applicants are reminded that each application is examined on its own merits and that the instant application is being examined using the revised utility guidelines.

9. **In case Applicant overcomes this utility rejection by providing convincing evidence in response to this Office Action, the following rejections will apply:**

Claim Rejections - 35 USC § 112, Second Paragraph

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 2 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 2 is indefinite in the recitation of "sequence that :....(b) hybridizes ...to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof".

13. This rejection was discussed at length in Paper No. 10, mailed on 5/7/2002.

14. Applicants argue that a nucleotide sequence is in fact also a nucleic acid molecule, therefore, one of skill in the art would understand that a sequence can hybridize. Also, Applicants argue that since the claim recites "the complement" as opposed to "a complement", it is clear that it refers to the complete complement.

15. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. A sequence, as indicated in previous Office Action Paper No. 10 is a graphical representation of the way nucleotides/amino acids are arranged in a molecule. Hybridization occurs only among molecules. Furthermore, the claim is indefinite in the recitation of "complement" for the reasons of record. Since no amendments have been made to the instant claim, this rejection is maintained. It is suggested that the claim be amended to recite more clear language, such as "an isolated nucleic acid molecule that: (a) comprises a nucleotide sequence that encodes.....; and (b) hybridizes under....to the polynucleotide of SEQ ID NO: 1 or the complete complement thereof". Correction is required.

Claim Rejections - 35 USC § 112, First Paragraph

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. Claims 1, 5 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

18. This rejection, which was discussed at length in Paper No. 10, mailed on 5/7/2002, was applied to claim 1 and is now applied to claims 5 and 8 for the reasons of record.

19. Applicants argue that the Examiner completely misread the written description requirement and submit that claim 1 satisfies the written description requirement since the structure of the polynucleotide of SEQ ID NO: 1 has been provided. Furthermore, Applicants argue, claim 1 meets the written description requirement set forth in *Univ. of California v. Eli Lilly and Co.*, since the polynucleotides of the instant invention are distinguished by structural features such as the sequence itself.

20. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. Applicant should note that the claims of the '740 patent in the *Lilly* case are limited by **both** structural limitations (the recited generic formula) and functional limitations (coding for human preproinsulin). As indicated in previous Office Action Paper No. 10, while it is agreed that the claimed genus of polynucleotides is defined in structural terms, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. In this case the genus of polynucleotides encompasses polynucleotides of <u>any function</u> which comprise at least 24 contiguous nucleotides of the polynucleotide of SEQ ID NO: 1. Thus, since there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation in such genus. As indicated in previous Office Action Paper No. 7 and 10, the state of the art clearly indicates that even proteins which share high sequence homology can have different function. See the teachings of Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995) and Broun et al. (Science 282:1315-1317, 1998) already discussed. Furthermore, even 98% sequence identical

proteins can have different function as demonstrated by Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) when comparing a melamine deaminase and atrazine chlorohydrolase. Based on the unpredictability of the art in regard to function and homology, it is clear that the claimed genus may include polynucleotides of many different and unknown functions. Therefore, the disclosure of only one species (SEQ ID NO: 1) is not sufficient to adequately describe a genus of widely variant species with many functionally unrelated polynucleotides. Thus, in view of Applicant's disclosure, one of skill in the art cannot reasonably conclude that Applicants had possession of the claimed invention at the time the application was filed.

21. Even if Applicants show credible, specific, and substantial utility for the polynucleotide of SEQ ID NO: 1, the following rejection applies. Claims 1, 5 and 8 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

22. This rejection, which was discussed at length in Paper No. 10, mailed on 5/7/2002, was applied to claim 1 and is now applied to claims 5 and 8 for the reasons of record.

23. Applicants argue that the Examiner has stated that the specification is enabled for the polypeptide of SEQ ID NO: 2 and that the lack of information as to function or structure of the polynucleotides claimed is irrelevant in determining patentability. Furthermore, it is Applicant's contention that if the polynucleotide of SEQ ID NO: 1 has been disclosed, one of skill in the art should be able to make the claimed polynucleotides. Applicants assert that insufficient guidance regarding the biological function or activity of the claimed invention should not be used as an

enablement standard based on established patent law. In addition, Applicants argue that the need for some experimentation does not render a claimed invention unpatentable. It is Applicant's opinion that arguments in regard to the unpredictability of the art in regard to amino acid changes and function were misplaced because there are numerous uses for the claimed polynucleotides which do not require knowledge of any functional aspects of the amino acid sequences. Applicants extensively argue that the specification is fully enabling since one of ordinary skill in the art can easily used the disclose nucleotide sequence to design probes and primers for the determination of expression patterns in tissues and that the specification does not need to provide what is well known in the art.

24. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. First, it is noted that the Examiner in previous Office Action Paper No. 10 stated that the specification "discloses" the sequence and function of the polypeptide of SEQ ID NO: 2 (page 8, paragraph 17). The specification does not enable the polypeptide of SEQ ID NO: 2 or its corresponding polynucleotide (SEQ ID NO: 1) in view of the utility issues already discussed. Even if Applicants can show utility for the polynucleotide of SEQ ID NO: 1, there is no enablement for any polynucleotide of any function comprising a fragment of at least 24 nucleotides of the polynucleotide of SEQ ID NO: 1. In regard to arguments related to insufficient information regarding biological activity, it is noted that the enablement rejection has not been applied to the claims using standards such as those applied by the FDA for drug approval. Instead, this enablement rejection was applied due to the lack of information as to how one of skill in the art can reasonably make and use the polynucleotides, as encompassed by the claims. It is agreed that while one of skill in the art can make an infinite number of

polynucleotides comprising at least 24 nucleotides of the polynucleotide of SEQ ID NO: 1, it is not routine in the art to make polynucleotides comprising at least 24 contiguous nucleotides of SEQ ID NO: 1 with the asserted function without any guidance as to which critical structural elements have to be present to display the desired function, as evidenced by Van de Loo et al. (Proc. Natl. Acad. Sci. 92:6743-6747, 1995), Broun et al. (Science 282:1315-1317, 1998) and Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001), already discussed. It is noted that polynucleotides that comprise at least 24 nucleotides of the polynucleotide of SEQ ID NO: 1 with serine protease activity is one of the subgenus encompassed by the claims. Even if one assumes that the polynucleotide of SEQ ID NO: 1 encodes a serine protease, as asserted by Applicants, there is no description of the function and use of polynucleotides comprising at least 24 contiguous nucleotides of the polynucleotide of SEQ ID NO: 1 having other functions in addition to serine protease. Furthermore, there is no information as to the critical structural elements required in a polynucleotide which encodes a serine protease.

In regard to arguments that the function is not required for the claimed polynucleotides since they can be used as probes or primers, while it is agreed that making such probes or primers is not undue experimentation, determining what is being targeted by such probes and the target's function constitute undue experimentation in view of the fact that one would have no information as to the probe's own function. Without knowing what the probe is targeting, it is unclear how one can be reasonably enabled to use the claimed invention as a probe. Thus, in view of the information provided, the lack of relevant examples, the lack of knowledge as to the critical structural elements required to display the desired activity and the unpredictability of the art in regard to function and homology, one of skill in the art would have to go through undue

experimentation to make and use the claimed invention in a manner reasonably correlated with the scope of the claims.

Conclusion

25. No claim is in condition for allowance.

26. Applicant's amendment which added new claims 5-8 necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Applicants are requested to submit a clean copy of the pending claims (including amendments, if any) in future written communications to aid in the examination of this application.

28. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with

the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
November 26, 2002

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600